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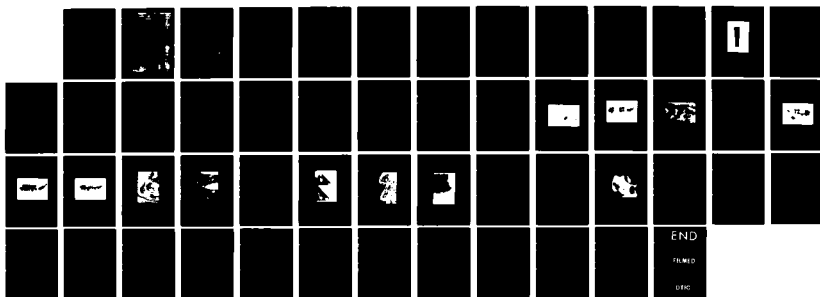
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SURGICAL TOOTH IMPLANTS, COMBAT AND FIELD

Annual Report

Craig R. Hassler, Robert H. Downes
Larry G. McCoy

July 15, 1983

Supported by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
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SURGICAL TOOTH IMPLANTS, COMBAT AND FIELD

by

Craig R. Hassler, Larry G. McCoy, and Nancy E. Arlin

SUMMARY

Long term implant studies of alumina tooth roots are being performed in both humans and baboons. The implants designed for this project are a single root rectangular design with serrations arranged for maximal stress distribution of occlusal loads. The implant is of a three-piece design. The serrated root portion is alumina ceramic. The upper two parts of the implant (post and core and crown) are conventional dental materials, usually gold. Roots are produced by grinding bisque fired alumina stock on a computer controlled milling machine. This technique provides high quality, high strength, and design flexibility. A series of graded sizes of implants have been produced. Serration depth was selectively reduced in smaller implants to provide the necessary bulk of ceramic. Extensive quality assurance has been performed on the implants intended for human use. Quality assurance procedures include: wet densities, visual inspection, and mechanical testing of test bars.

Long term baboon implants were terminated after 8 years, with an average implant residence time of 5.25 years. A high success rate has been maintained, as reported previously. Some implants had functioned successfully for more than seven years. The animals appeared to severely stress the implants thus providing an extreme test for the implants. There have been fractures of ceramic roots in the baboons. Fracture was the principal cause of post reconstruction implant failure. These fractures have been uniquely isolated to one batch of ceramic roots produced for baboons in 1976. Consequently, we suspect that poor material strength was responsible for the failures. Since that time, improved ceramic processing techniques have dramatically increased the flexural strength of the implants. This improvement minimizes the probability of future fractures.

In humans, implants have been performed using three different techniques. Of the three techniques, repeatable and satisfactory results appear to be obtainable when the implant is placed flush with the alveolar bone. This technique apparently isolates the implant sufficiently from mechanical stresses so that ingrowth into the implant serrations can occur. If the implant remains rigidly fixed in bone throughout the ingrowth and reconstruction phase, long-term prognosis for implant success is excellent. Consequently, initial ingrowth is the most critical phase of the implant procedure. Criticality of the initial ingrowth phase was also observed in baboons.

The human implant series is approaching completion of the active implantation and reconstruction phases. Long-term functional evaluation of patients will be continued.

FOREWORD

This study has been conducted at Battelle's Columbus Laboratories utilizing the staff and resources of the Health and Environmental Sciences Section and the Ceramics Section. The clinical portion of this study has been conducted at The Ohio State University College of Dentistry.

This is the thirteenth report of progress under Contract No. DAMD-17-82-C-2020, "Surgical Tooth Implants, Combat and Field". The principal investigator for this research was Dr. Craig R. Hassler. Ceramics research was directed by Mr. Larry G. McCoy. The human studies have been under the direction of Dr. Nancy E. Arlin and Dr. William Wallace in the clinical facilities of the Ohio State University College of Dentistry. Clinical research was conducted under a protocol approved by The Ohio State University Human Subjects Committee. This research has been performed in accordance with an investigational device exemption obtained from the FDA. Animal research, conducted at Battelle-Columbus has followed the guidelines of the "Guide for Laboratory Animals Facility and Care" as promulgated by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences, National Research Council.

QUALITY ASSURANCE STATEMENT

This study was inspected by the Quality Assurance Unit and reports were submitted to management and the principal investigator as follows:

<u>Phase</u>	<u>Date</u>
Clinical observations, pictures, X-rays, blood collection, body weights, flossing and brushing of teeth.	3/28/83
Necropsy	4/7/83
Review of annual report	8/9/83

This study was done in compliance with the Food and Drug Administration's Good Laboratory Practice Regulations (21 CFR 58). To the best of my knowledge the methods described were the methods followed and the data presented accurately represent data generated during the study.

Ramona Mayer, Director
Quality Assurance Unit
Biological Sciences Department

BACKGROUND

In the last several years a new generation of dental implants has evolved. These devices are designed to be rigidly affixed by bone ingrowth and provide minimization of stress usually by serrations(1-4) or pores.(5-6) Generally, these implants are designed as single freestanding prostheses. Several biocompatible materials have been utilized including plastics,(7) metallics(6), and ceramics.(1,2,3,8-18,22-24,26-29) Our laboratory has specialized by using alumina (Al_2O_3) ceramics incorporating a serrated design. In the past 12 years we have developed a combination of material, design, and technique components which appear promising. It should be noted that all three components (design, material and technique) are of importance if an implant system is to be successful. Failure of any of the three components can be detrimental. A serrated ceramic implant system based upon these principles is under test in our laboratories. Implant experience in animals exceeds 7 years of function. On the strength of the animal experiments, a clinical study was undertaken to evaluate how much of the technology was relevant to the human situation.

The lower portion of our three-piece implants are produced from alumina (Al_2O_3) (Figure 1). This portion has large serrations into which bone ingrowth has been demonstrated.(4) The implant illustrated in Figure 1 has smaller serrations at the crown end of the root to increase the strength of smaller sized roots in these critical areas. The upper two portions of the implant: post and core and crown - are cemented after ingrowth to allow function. The three-piece design allows minimization of occlusal stresses and strains on the implant to facilitate bone ingrowth. An analogous situation is seen in the healing of long bone. It is assumed that, as in long bone, an orderly transition through a sequence of gradually stiffer bone materials proceeds (hematoma → connective tissue → woven bone → compact bone). The maximal strain which any of these tissues can withstand must not be exceeded if healing is to proceed to completion.(21) Consequently, strain upon the implant-bone interface must be minimized early in the healing process if bone formation is to occur. Once the implant is stabilized by ingrowth, the large implant surface area at right angles to the principal load axis of the implant

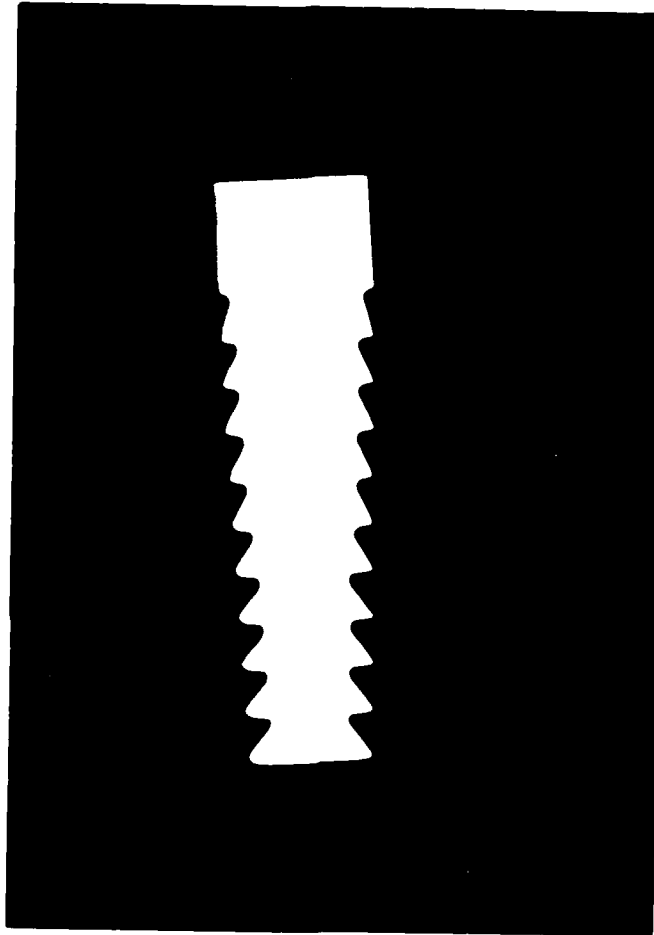


FIGURE 1. SERRATED ALUMINUM OXIDE DENTAL IMPLANT

This photograph shows a rectangular root with smaller serrations at the top for increased strength. Not visible is the post hole in the center of the implant. A prefabricated post and core is cemented into the hole. A clinical crown is then cemented to the post and core.

is intended to maintain bone stresses below a level which produces resorption of bone. Attempts to quantify these stresses have been made in this laboratory.⁽⁹⁾ This information is not specifically for alveolar bone; however, it serves as a guide in an area where no direct information is available. As demonstrated by histologic data collected on this project⁽²⁾, the hypothesis appears to be viable bone can exist successfully in direct contact with a functional implant.

The above mentioned parameters, unique to this design, are the serrations and three piece construction. They are the two major determinants for design success. A secondary design parameter which has proven useful is the use of a size graded series of implants. This gradation allows optimal fit into the available site. Numerous sizes have been produced for the clinical studies. In practice several of these sizes are not used, but they are available when required. Both rectangular and elliptical implants were used in the baboons. However, the rectangular shape appeared to provide a better initial fit. Consequently, this design is being used exclusively in human clinical trials.

The shape and size flexibility of the rectangular design is especially crucial when placing implants in fresh extraction sites. A circular implant will rarely provide adequate initial stability in a fresh extraction site. Furthermore, implant size is limited by the buccal-lingual dimension with a circular design. A disadvantage to the rectangular design is that more operator skill is required to initially place the implant than would be required with a circular implant.

The method of producing roots by contour grinding, on a computer controlled milling machine, has allowed for flexibility not only in size, but in other design changes. In a research protocol, this ease of flexibility has been an asset and will continue to be our method of root manufacture.

The animal experiments have recently been terminated and the long-term implant success in animals is encouraging. Success for a similar time span in humans is necessary to determine the true success of the implant.

METHODS

Fabrication of Tooth Roots

During this project year, fabrication techniques identical to those used previously were employed. The powder used for fabrication is Reynolds Aluminum Company's RC-HP-DBM. This is a high purity, dry ball milled powder having a median particle size of approximately 0.5 microns. The methods for production of the tooth roots has been reported previously(27,28). Briefly, the processing procedure used is as follows:

- (1) Hydrostatic pressing granulated material at 50,000 psi to form preform rods nominally 125 mm long by 14 mm diameter
- (2) Bisque firing preform rods at 1120 C for 2 hours
- (3) Contour grinding tooth roots
- (4) Hand finishing tooth roots
- (5) Final sintering at 1540 C for 1-1/2 hours.

A quality assurance program is utilized on all roots destined for clinical trials. The details of this program have been published in our previous reports(27,28). Briefly, this program consists of:

- (1) A method of traceability which allows each root to be identified as to raw material, size, and time of manufacture.
- (2) Manufacture of test bars, which are produced for each batch of roots. Presently flexural strengths averaging 70,000 psi are being obtained.
- (3) Microscopic examinations of each root by both transmitted and reflected light.
- (4) Wet density measurements of representative implants from each group.

Twenty-three implants ranging in size from 4x4 mm to 5x8 mm were completed this year to provide sufficient implants for the completion of the clinical study.

Investigational Device Exemption Application

To place this study in compliance with 1976 modifications of the Pure Food Drug and Cosmetic Act, application for an Investigational Device was made to the FDA. This Exemption (IDE) allows clinical research of experimental devices that have not yet been commercially produced. The exemption provides necessary freedom for a product to be adequately evaluated. Strict reporting requirements are placed upon the investigators. The clinical data collected must be reported to the FDA at least annually. This exemption does not supplant the authority of the local human subject committee. The various reporting requirements required by the FDA have been complied with. The requested exemption was obtained for this project in January of 1980. The project has been reviewed and approved annually by both the FDA and the Ohio State University Human Subjects Committee.

Baboon Implant Procedures

Animal implant procedures have been performed in the adult, female baboon. Only two implants were performed this project year. They were solely for the purpose of familiarizing new clinical personnel with the procedure. The procedures used in this study are briefly outlined below. Typically, following extraction the tooth socket, either molar or pre-molar, was shaped using a bone burr. A socket was formed by a continual fitting procedure. The root was firmly tapped into the alveolar bone until flush with the bone. The root was given no further attention, however, the animal received prophylactic antibiotics immediately post-surgery and a soft diet for two weeks. The root implant site was observed periodically for three months. Radiographic examination and manual palpation indicated if the root was adequately stable for reconstruction. A similar procedure was used to implant roots in edentulous sites.

Restoration of the implants was facilitated by prefabrication of a gold post and core prior to implantation. Following adequate stabilization by bone ingrowth into the serrations (at approximately 3 months), the post and core was cemented into place. Impressions were taken. A gold crown was fabricated and cemented into place. Care was taken to provide correct

occlusion. The implants were periodically examined and documented by radiographs and photographs.

Additional Animal Techniques

Clinical chemistry, hematology and parasite analyses were continued periodically and at experiment termination. One half of the animal colony (animals 409, 709, and 712) were scaled, flossed and then brushed for 3 minutes with a 2 percent solution of chlorhexidine gluconate four times prior to necropsy. (The teeth were scaled only initially.) The treatments were at approximately weekly intervals.(30)

For histomorphometric analysis of bone growth rates, all animals were tetracycline double labeled in a 2-7-2-7 pattern prior to necropsy.(31)

Baboon Husbandry

The animals housed in this study were individually caged in one room of the Battelle-Columbus animal facility. The animals were fed Purina monkey chow twice daily. One daily meal consists of the chow pre-moistened and softened, whereas the other meal was the same chow in the as-received dry state. Water was ad libitum, via drinking bottles. The room environment was maintained on a 12-hour light/12-hour dark cycle. Temperature is maintained between 72-76 F. Humidity was maintained between 40-60 percent RH. Visual observations of the animals was recorded twice daily. Any unusual observations were reported to the veterinarian in charge and the principal investigator. For evaluation procedures the animals are tranquilized with Ketamine® prior to removal from their cages.

Human Implant Procedures

Rectangular implants are placed in edentulous, or fresh extraction sites. Roots are placed where they will function as single free-standing implants when reconstructed. Under local anesthetic, implant sites are prepared using bone burrs placed in a low-speed contra-angle air turbine handpiece with

sterile saline cooling. A continual fitting procedure is used. Final placement of the implant is via tapping with a mallet to provide a stable interference fit. The root implant site is observed visually and radiographically throughout the study. Normally a gold post and core is prefabricated for each implant. The patients are observed periodically until the implant is rigid or exhibits minimal motion. At that time, the post and core is cemented and a clinical crown fashioned. Periodic examination of the patient continues following reconstruction. All clinical studies are performed at The Ohio State University College of Dentistry, in compliance with a protocol approved by the Ohio State University Human Subjects Committee and the FDA Bureau of Medical Devices.

Three variations of implant technique have been employed: In the first group, implants were surgically placed so that the uppermost serration was just covered by the crest of the alveolar ridge. Consequently, about 3 mm of implant was left protruding above the ridge. The first 25 patients were implanted in this fashion.

A second group of six patients' implants were prepared with integral post and cores. The implants were partially isolated from occlusal loads by orthodontic stay wires attached to adjacent dentition and a methacrylate resin cap over the top of the implant.

A third group of twenty-four patients was prepared in which the top of the root was placed flush with the alveolar crest. Whenever possible a muco-periosteal flap was placed over the top of the implant. This flush implant technique is the only one presently in use. Both anterior maxillary and posterior mandibular sites are included in this third group.

RESULTS

ANIMAL STUDIES

On April 7th and 8th 1983, the remaining six baboons in the colony were terminated, utilizing an intravenous injection of sodium pentobarbital. A gross necropsy was performed. Forty-eight tissues were collected from each animal. The tissues were preserved in 10% neutral buffered formalin and forwarded to the Army for histopathologic analysis. Tissues previously removed from early death animals were also sent to the Army for analysis. At the time of this annual report, histopathologic analysis results were not available.

At necropsy, duplicate tissue samples were collected and frozen. These samples will be analyzed via ion absorption mass spectrometry for the accumulation (if any) of aluminum ion in body tissues.

Summary Analysis of Baboon Implant Data

For the purposes of this analysis, all implants have been classified according to their "final" status at time of death or necropsy. Some implants underwent a complicated course involving several different procedures. This analysis is intended as a "worst case" analysis where each implant is categorized in according to its least favorable outcome. This analysis includes all implants placed in the 9 animals retained at Battelle for the long term dental implant study.

Forty-three attempts were made to place implants. Thirty-eight, or 88% of the implants survived the initial ingrowth phase. All of these ingrowth failures were early implant attempts (Prior to 1977). Three of the five failures occurred in one animal. This animal was subsequently successfully implanted, suggesting that technique improvements or operator experience may be failure contributing factors. Suspected failure modes included: fracture of the buccal plate, and placing the implants too high relative to the alveolar crest.

Of the 38 implants which were retained, 24 or 63% were totally functional and complete implant units at necropsy or animal death. The 14

implants not complete at experiment termination were distributed in the following manner:

- 8 implants fractured while in service
- 1 implant lost its post and core and crown
- 1 implant was fractured during an attempted removal
- 4 were never restored

These implants were analyzed in the following manner: all fractured roots were from the same processing batch. No implants manufactured either before or after that particular batch have ever fractured. Consequently, poor material quality is suspected. These early implants were not put through a quality assurance program as is the practice with implants prepared for clinical study. The implants that did fail experienced an average of 3.27 years ± 1.49 years before failure. Extreme crown wear seen on all baboon dental implants indicated that the animals severely stressed the devices. But, the actual contribution of severe treatment to implant fracture cannot be determined.

The Post and Core and Crown loss is suspected to be due to faulty zinc oxyphosphate cement, and probably not related to a difficulty with the implant per se. Suspected cement failures were seen in other implants which were recemented and are classified elsewhere. For example: Area 18 in animal 469 lost its crown after 3 years. The implant remained in function via the post and core until two months before necropsy when the implant fractured. This implant is counted as a fracture failure in this analysis. A similar example was seen in animal 713 area 20. A crown was lost due to cement failure after 2 years. The crown was recemented. However the implant eventually fractured and the implant was categorized as a fracture loss. A total of 3 implants exhibited cement failures, were reconstructed and went on to eventually fail, due to fracture.

One implant (A19 animal 712) presented an interesting case history. This implant never became stable. After 16 weeks, a removal was attempted, at which time the implant fractured. The remaining root, now below alveolar crest, became rigidly fixed in the bone and remained. This implant compounds the analysis since technically it is a loss, but still remained in the animal. Consequently, the implant was placed in a unique category. A similar incident

was noted in animal B, area 29. The implant was placed in function earlier than usual. Normally, at least 90 days is permitted to elapse. But in this case only 68 days elapsed before reconstruction was undertaken. The implant loosened progressively. Twice, in the next 2.25 years, crown height was reduced to minimize function on the implant, but the implant remained mobile. Eventually, after 4 years, the implant fractured. The root segment of implant, now totally removed from any function, became rigidly fixed in the bone and remained so. These two cases suggest that a mobile root can eventually stabilize, but only in the absence of external stresses.

The four implants, never restored, were placed late in the program to train new clinicians for the clinical program. The residence time of these roots was too short (with one exception) to judge whether they would have been successful or not.

The 24 implants termed totally successful experienced an average implant residence time of 5.26 years \pm 1.49 years. It is significant that, with one exception, all baboon implants that become rigidly implanted remained rigidly fixed. A very optimistic analysis could state a 33 out of 34, or 97% success rate for stabilized roots, if various mechanical failure modes such as implant fracture and cement failure are discounted. On the other hand a pessimistic analysis of the data could state that only 24 of the 43 roots or 56% were totally successful. The percentage could be even further reduced if crowns with extensive wear are considered failures. Obviously, the true success of the implant system is between the above stated percentages. The perception of success depends upon the analysis criteria employed. It is most important to indicate that the data strongly supports the hypothesis that a dental implant of this design can become rigidly fixed in bone and satisfactorily distribute the occlusal stresses on an extended basis.

Early Deaths

A total of three early deaths were observed among the nine baboons in the long-term study. On February 26, 1982, baboon 714 died following an illness of relatively short duration, despite an effort to save the animal. A ceramic root had been recently implanted on December 10, 1981, utilizing the

buccal flap technique. The baboon was placed on prophylactic antibiotic therapy and a soft diet, which is standard procedure following implant surgery. Daily observations disclosed the baboon was eating little, which is not uncommon following surgery, so fruit was supplemented to its diet as an inducement to increase food intake. However, the low level of consumption continued. The animal's condition deteriorated, so a physical examination was performed on December 16, 1982 to determine the cause. The examination disclosed that the animal had torn off the buccal flap covering the most recent root implant. Antibiotic therapy was immediately resumed and additional tests were performed, but the baboon's condition continued to deteriorate until it finally died. The gross necropsy of the baboon gave inconclusive evidence as to the cause of death. The histopathology evaluation of major organ systems following necropsy indicated systemic septicemia as the probable cause of death. The point of origin of the infection was not ascertained.

On September 18, 1982, Animal 713 was found dead in her cage. There were no prior clinical signs prior to the death. Gross pathologic examination revealed no abnormal tissue. The abdomen of the animal was found distended at the time of necropsy. The pathologists diagnosis indicates acute gastric distention as the cause of death. This condition of unknown etiology is occasionally noted in primates and dogs. The animals' stomach will distend abnormally, usually following a heavy meal and or exercise. Distention of the stomach apparently interferes with the venous return. Animals usually die within 4 hours of the first clinical signs.

The rapid and devastating nature of this unusual syndrome can kill animals even between periodic clinical observations. Unfortunately, this animal became ill at night, between 12 a.m. and 6 a.m. This is the first recorded incident of this syndrome, in a baboon, in our laboratory. However, we have experienced several deaths in Rhesus monkeys attributed to this syndrome.

On November 11, 1982, Animal 711 died during exploratory surgery. A week prior to this unsuccessful surgical intervention the animal was noted to be lethargic and refused food. The animal did not respond to any conventional therapy. The contents of the abdominal cavity were rigid when palpated. Due to the animals continually deteriorating condition, an exploratory laparotomy

was performed. The procedure revealed massive adhesions and severe endometriosis. Due to its weakened condition, the animal did not survive the surgery. The surgical findings were confirmed by necropsy. No other pathology was found.

Tissues from 711 and 713 were sent to the Army for histopathologic analysis. The dental implants were removed and retained at Battelle for histologic analysis. These three deaths appear to be unrelated to the presence of dental implants. However, the death of animal 714 may be attributable to surgical error.

Clinical Examples of Baboon Dental Implants

Photographic examples of long term implants in the animal study are shown in Figure 2. These implants (Baboon 469, A29, and A30) were in place for 7.34 years and 7.71 years respectively. The implants were rigid and in occlusion at necropsy. The gingival health was excellent, perhaps due in part to the chlorohexidine gluconate treatment. Extensive wear was seen on the crown surfaces. This wear is typical of long term Baboon implants. Aluminum staining on Baboon teeth indicated chewing on the cage bars. Presumably, the accelerated crown wear was due to this chewing activity.

Figure 3 is a post necropsy radiograph of the excised mandible of Baboon 469. This radiograph shows excellent hard tissue detail since interfering soft tissue has been removed. Most striking is the density of bone about the implant. All rigid implants demonstrate this increased radio-density. This increase in density is interpreted as a response to the stresses induced in the bone by the functional implants.

Figure 4 is another clinical example of long term function in a Baboon. These implants are also from animal 469. The total implant time of these roots was 7.34 years. As in the previous example, these implants exhibited excellent gingival health. There is a thickening of the gingiva, a cuff like formation, about the buccal aspect of the implant. This cuff of gingiva was seen adjacent to several of the Baboon implants. It appears to be a response to poor gingival attachment.

Figure 5 is a post necropsy radiograph of A18, A19, and A20 in Baboon 469. This is the same area as shown in Figure 4. Dense bone,

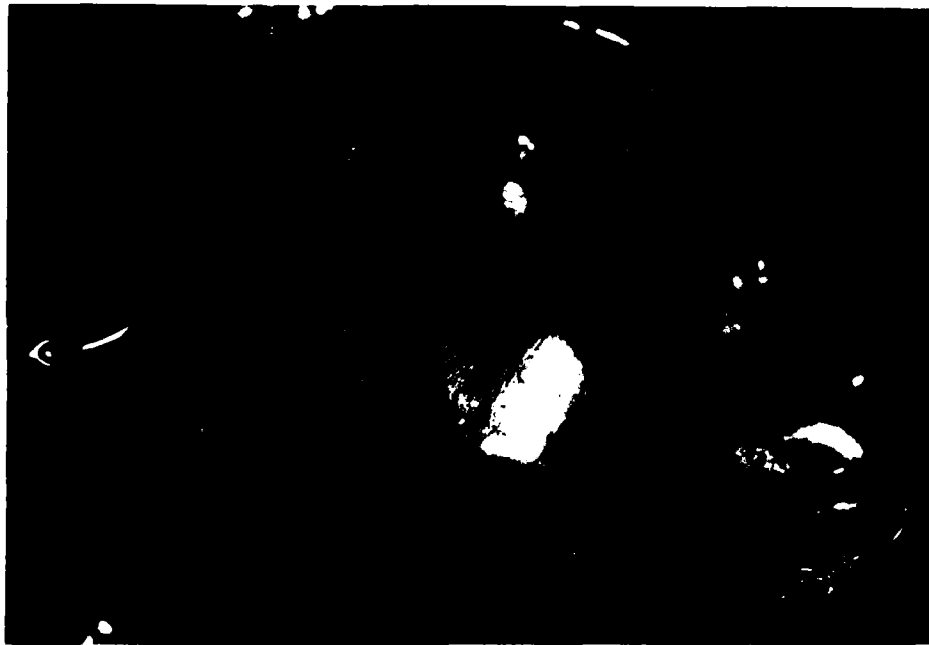


FIGURE 2. CLINICAL PHOTOGRAPH OF A29 AND A30 IN BABOON 469
AT NECROPSY

These particular implants had been implanted for 7.34 and 7.71
years prior to Necropsy. The crowns exhibit extensive wear.

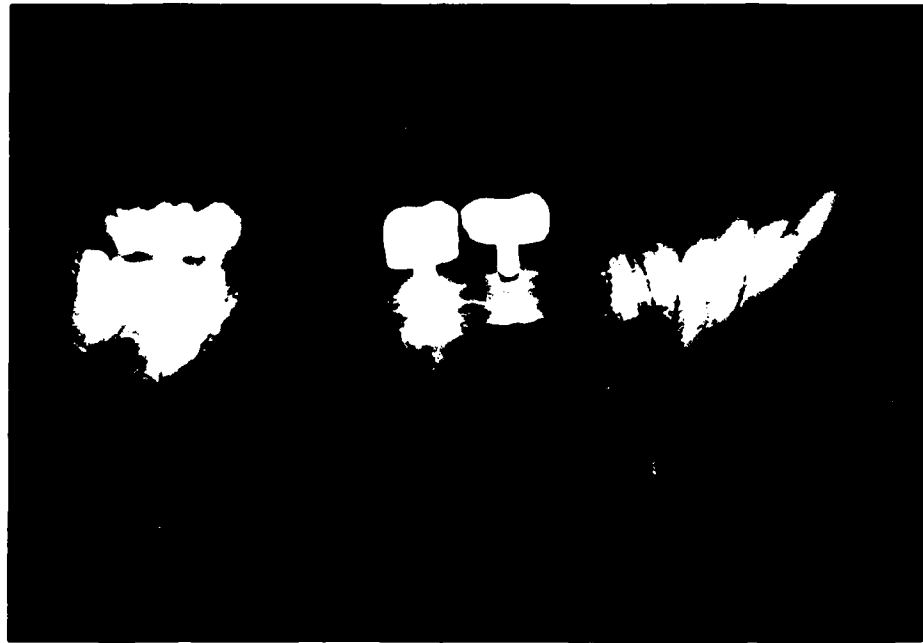


FIGURE 3. POST NECROPSY RADIOGRAPH OF A29 AND A30 IN BABOON 469

This radiograph illustrates the dense bone formation typically seen around the rigid long term implants. The serration detail is obscured by the bone formation. Bone appears denser at the alveolar crest. Crestal height was maintained through the life of these implants.



FIGURE 4. CLINICAL PHOTOGRAPH OF A19 AND A20 IN BABOON 469 AT NECROPSY

These two implants were in place for 7.71 years. The crowns exhibit wear and the gingival cuff often seen on multiple baboon implants is present. A distal implant in A18 fractured approximately 2 months before necrosis.

obscuring the serration detail can be observed about the implants. Vertical bone loss is evident about the implants. The bone loss is dramatic about the fractured implant in A18. The vertical loss about A19 and A20 implants appeared subsequent to the implantation in A18. Sequential radiographs in the 12th report²⁹ illustrate this point.

Figure 6 is a post necropsy radiograph of mandibular implants in A29 and A30 of Baboon 712. These implants were in place 4.93 years. In this example, alveolar crest was well maintained. As is typical with these implants, the bone appears denser near the alveolar crest. Figure 7 is a post necropsy radiograph of two implants placed 1.31 years (A31) and 39 days (A29) prior to necropsy. Neither of these implants were ever reconstructed. Note that the serrations of the implants are still plainly visible, especially when compared to the long-term function implants. The bone has never increased density about in these nonfunctional implants. Comparison of functional implant radiographs (Figures 5 and 6) to this nonfunction implant radiograph suggests that the increase observed in bone density is a response to the functional stresses.

Histologic Analysis of the Bone-Implant Interface

Analyses of the bone-implant interfaces is now in progress for implants retrieved from necropsy as well as early deaths. Only a limited number of preparations were completed in time for inclusion in this report.

Figure 8 is a photomicrograph, showing serration detail from A29 of Baboon 469. This particular implant was in place for 7.71 years. This represents the longest implant duration of the study. Note that dense, well organized bone mixed with some connective tissue has totally filled the serration. There appears to have been close apposition between bone and implant. The gap at the interface was caused by the slide grinding process.

Figure 9 shows serration tip detail around the same implant in Figure 8 (A29, Baboon 469). Well formed bone totally surrounds the serrations with no apparent interveining connective tissue. Similar dense bone ingrowth was previously demonstrated after 2 years. This data was presented in the 8th report².

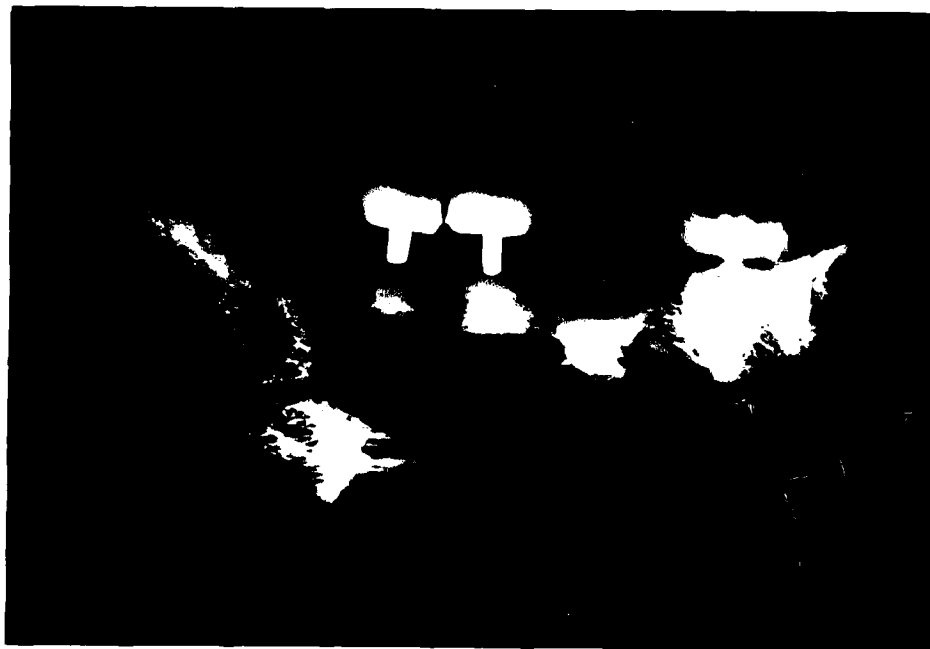


FIGURE 5. POST NECROPSY RADIOGRAPHIC OF A18, A19, AND A20
IN BABOON 469

This radiograph corresponds with implants shown in Figure 4.
Vertical alveolar bone loss is evident.



FIGURE 6. POST NECROPSY RADIOGRAPHS OF IMPLANTS IN A29 AND A30 OF BABOON 712

These implants have been in place for 4.93 years. Alveolar crest height was well maintained around the implants. The increase in bone density and the pattern of the density increase is typical.

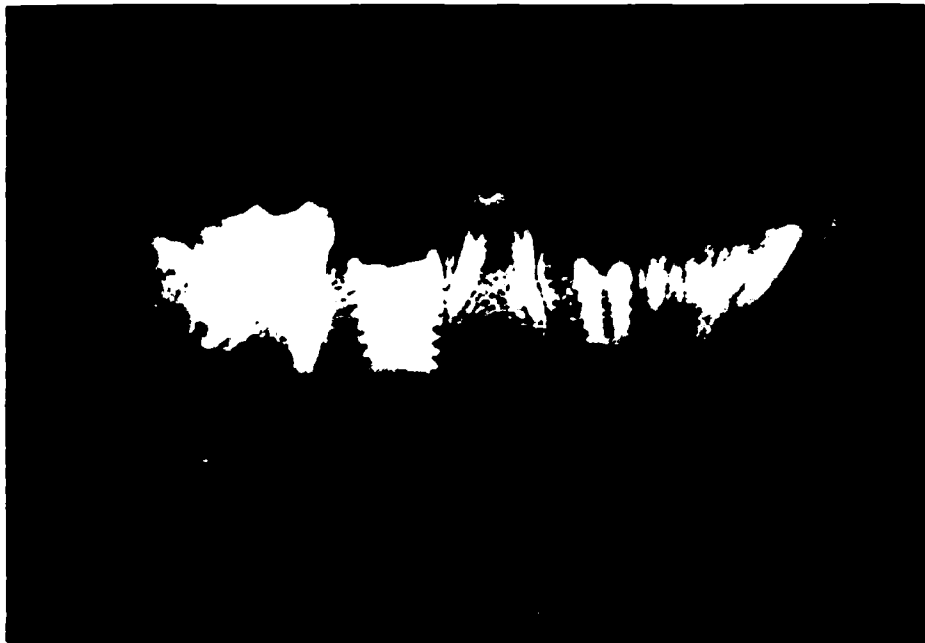


FIGURE 7. POST NECROPSY RADIOGRAPH OF NON FUNCTIONAL IMPLANTS
IN A29 AND A39 OF BABOON 715

These two implants were in place for 39 days and 1.31 years respectively, but they were never in function. Note that the bone density has never increased around these implants as is typically observed in functional implants (see Figures 5 and 6).



FIGURE 8. PHOTOMICROGRAPH OF SERRATION DETAIL A29 BABOON 469

This relatively high magnification view shows well developed bone, with lacunae and haversian systems. There are areas of connective tissue interspaced along the biomaterial interface. The implant has separated from the bone during preparation.

This is an implant representative of the longest implant duration observed in this study, 7.71 years.



FIGURE 9. PHOTOMICROGRAPH OF IMPLANT A29 BABOON 469

This view demonstrates extremely dense bone totally surrounding a serration tip. The interface between bone and ceramic appears extremely tight, with no observable interface of connective tissue. This implant was in place for 7.71 years.

Figure 10 shows an example of dense bone ingrowth around implant serrations after 6.16 years (Baboon B-A19). As in the previous examples, a dense ingrowth of bone can be observed into the serrations. This basic fuchsin stained slide emphasizes the connective tissue.

Figure 11 presents a somewhat different appearance, in that bone is not as dense. However, this is a maxillary implant in place for 2.12 years (Baboon 713, A7). There appears to be a thin layer of bone adherent to the ceramic, with large void spaces. This bone architecture is similar to that observed mesial and distal to some mandibular implants. Since our experience with maxillary implants is limited, it is premature to describe this result as typical of a maxillary site. Clinically this implant is rigid.

Figure 12 is an example of double tetracycline stained bone. The photomicrograph shows the detail of one serration from Baboon B, A19. This implant was in place for 6.16 years. Note the double circular rings about the large haversian canal in the intra serration bone mass. The distance between the two labels is a measure of the bone formation rate which occurred in one week. Note that there does not appear to be any significant bone formation occurring at the bone-implant interface. This implies a stable and mature bone at the interface. Since bone is always remodeling some areas of the interface must be remodeling. However, the percentage of surface area undergoing a remodeling may be low enough that the chances of observing interface remodeling are remote. A judgement cannot be made until more samples are available for analysis.

Clinical Chemistry and Hematology Results in Baboons

Throughout the project history hematology and clinical chemistry data were collected on all animals, at approximately 3 month intervals and prior to necropsy. To date no value has shown an apparent significant alteration from baseline with the exception of values from animal 711, which periodically had low hematocrit. The parameters measured were: Glucose, BUN, Chloride, Bilirubin, Alk. phos., SGOT, SGPT, Creatinine, Na, Ca, Mg, K, Hemoglobin, Hematocrit, WBC, RBC, MCV, BANDS, SEGS, EOS, BASO, Lymph, Mono, Platelets, Retic and Pro-time. A more complete analysis of this data is planned.



FIGURE 10. PHOTOMICROGRAPH OF IMPLANT A19 BAROON B

This preparation, like previous examples shows dense bone filling virtually all available space in two serrations. The staining process emphasizes connective tissue at the interface as well as in voids. Some slight separation, probably due to processing can be observed along portions of the interface.



FIGURE 11. PHOTOMICROGRAPH OF IMPLANT A7 BABOON 713

This maxillary implant, in place for 2.12 years shows less dense bone architecture. The ceramic was removed during preparation. However, there appears to be a thin layer of connective tissue along most of the interface.



FIGURE 12. DOUBLE TETRACYCLINE LABELED BONE INGROWTH DETAIL
A19 BABOON B

This animal was labeled with tetracycline twice at weekly intervals prior to necropsy. The only real evidence of bone remodeling observed thus far is within the large haversian canals, and not at the implant interfaces.

Clinical Studies

The clinical portion of this project has involved the implantation of rectangular ceramic roots in 55 patients. The clinical study commenced in August, 1978. The roots have been implanted using three different techniques. In the first 25 patients, roots were implanted in mandibular areas with the first (or uppermost) serration flush with the alveolar crest. This implant height was dictated by the post and core design, in which the gold overlaps the outside of the root structure and extends downward into the gingival sulcus. In the human, the implant was placed high enough to allow post and core seating without bone removal. Hence, the implant was placed higher than in baboon studies. Success in baboons, even when the implants were left to protrude slightly above the alveolar bone level, gave us confidence that in the "cooperative" human subject this procedure would be acceptable. In the first 25 patients, mandibular molar and premolar sites were used. Seventeen were healed sites and 8 were fresh extraction sites. All implants were periodically observed by clinical observation and X-ray. All implants were rigid at the time of surgery, by virtue of the interference fit produced by tapping the implant into place. All implants exhibited some degree of buccal-lingual mobility within the first 1 to 3 months post-implant. The degree of mobility and the cause of the increase in mobility was highly variable, but typically 1/2 mm or less mobility was observed within that time period. Sixteen of the 25 patients exhibited a subsequent decrease in mobility with time. Of the original patients, six are still in function with buccal-lingual mobility ranging from 0-3/4 mm. The average implant time in these patients is 4.41 years. The average restoration time is 2.54 years. The longest implant time is 4.88 years. This data should be viewed cautiously since approximately half of these remaining implant patients have not been available recently for follow-up. However, it is obvious that the implant results obtained in group I are not satisfactory.

There have been some notable successes in this group. Some patients' implants have become totally rigid and appear to be identical to

the baboon studies in their clinical course. Figure 13 is an example of one such implant. This posterior mandibular implant has been implanted for 4.65 years and in function for 3.85 years. The clinical appearance of the implant has remained stable throughout the study. The bone height appears to be remaining stable. This particular implant exhibited some buccal-lingual mobility early in its course, but the implant became completely stable prior to reconstruction. This reduction of implant mobility, clearly observed in at least two patients indicates that stability can be regained, however, this is probably the exceptional case.

Of the failed implants in this group, 12 were restored and 5 failed prior to restoration. In the restored group of failures, average implant time till failure was 2.06 years. The range of time to failure was 1 year to 3.13 years. With the unrestored implants, the average implant time at failure was 1.35 years. The range of nonrestored failure time was 2 weeks to 2.25 years.

The typical failure process observed was a slow increase in mobility over two years. When mobility reached 1 mm buccal-lingual, with rotation present, the implant was removed to prevent unnecessary bone loss. Two patients had infection noted at implant removal time. Seven patients near removal time indicated some degree of soreness when biting hard. Generally gingival health remained excellent in all patients regardless of the state of failure. Most patients utilized the implants as functional and aesthetic devices up until the time of removal. Several patients had to be convinced of impending implant failure, since they were satisfied with the devices. All patients with implants removed have gone on to heal uneventfully.

In view of the difficulty of obtaining stability in the first group of patients, the next series of six patients (group II) were performed using orthodontic devices to stabilize the implant to adjacent teeth. Orthodontic bands were fitted to adjacent teeth and connected by wires. An acrylic cap was fitted over the top of the implant to support and protect the implant.

The patients were implanted in the posterior mandibular areas, 5 in healed sites, and 1 fresh extraction site. The fresh extraction site implant never stabilized and was never restored. The implant was removed at 35 weeks post-surgery when rotation was observed.



FIGURE 13. CLINICAL PHOTOGRAPH OF POSTERIOR MANDIBULAR HUMAN IMPLANT

This is an example of a success from the first group of patients where the root was allowed to protrude above the alveolar bone during ingrowth. Despite this poor technique, the root has become rigid, there has been minimal bone loss, the bone density has increased around the implant, gingival health is excellent and the prosthesis is functional. This implant has been in function for 3.85 years.

Four of the healed site implants remain in function, but they all exhibit approximately 1/2 mm of buccal-lingual mobility. The average implant time in this group is 3.02 years, \pm .12 years with a range of 2.92 years to 3.13 years. The average restoration time is 2.35 years \pm .07 years. The one functional failure in this group occurred after being implanted for 1.75 years and functional for 1.27 years. Even though these implants are functional, aesthetic, and well accepted by the patients, they are a less than optimal result. Our previous experience indicates that the long term prognosis for these implants is poor. One should anticipate that these implants will all eventually fail. However, the time to failure may be longer than in group one, since the mobility of implants in this group is not changing dramatically. This group of patients has been more cooperative than group I, and consequently these follow-up data are more reliable. The 4 implants still in function remain in the same condition as described last year⁽²⁹⁾.

In light of the less than optimal results of the previous research groups, a third group of patients (group III) was started. This group was to assess if a deeper placement of the root would offer additional protection from mechanical "stress" and allow the initial mechanical stabilization of the implant to proceed to a long term rigid situation; as commonly observed in baboon studies, but infrequently observed in prior human studies. The implant design as utilized in group I studies prevented flush placement of the implant. Since bone and attached gingiva would have to be removed to seat the overlapping post and core; the gold overlap (or coping) was removed, thus creating a post and core flush with the exterior surface of the alumina. Mechanical testing indicated that this removal of coping did not reduce the mechanical strength of the root-post and core attachment⁽²⁸⁾. Consequently, post and cores for group three studies do not have an overlapping gold coping. Additionally, the ceramic root portion has been modified to facilitate flush placement.

To date, 25 patients have been implanted in both fresh and healed sites using the flush implant technique (Group III). Implants have been placed in mandibular bicuspid and molar areas and six have been placed in maxillary anterior and bicuspid areas. A mucoperiosteal flap was used, wherever possible. Five of the 24 implants have failed. The time until

failure ranged between 3 weeks and 41 weeks. There was no apparent consistency to these failures.

The remaining 20 implants have been implanted for an average of 1.38 years \pm .72 years. The range of implant times is from 1 week to 2.23 years.

Ten of these implants have been successfully restored. The average restoration time is .64 years \pm .78 years. None of these implants show any significant bone loss. One of these implants has exhibited minimal mobility.

Late in the implantation of group III patients, improved instrumentation became available. Files, shaped with implant cross section dimensions, plug gauges and special burs were produced. These tools subjectively appeared to facilitate the implantation. However, none of the implants placed using this improved instrumentation, have yet been reconstructed. Consequently, judgement should be reserved as to the value of these devices.

Eight potentially successful patients remain to be restored. Two of these patients exhibit some mobility and their success is questionable. Since there are a large number of implants awaiting restoration, and the average function time is short, the long term success of group III is hard to judge. However, the results are obviously superior to those obtained with groups I and II.

The data tend to support the observation made in baboons and group I. Initial stability of the implant is the most significant obstacle to long term implant success. This hypothesis will probably be strongly supported by the group III human studies when more data is available.

Parametric Analysis

To expand our understanding of the mechanics between the dental implant and the bone, a mathematical analysis of the implant has been completed. The method being used is finite-element analysis. This laboratory, as well as the biomechanics community in general, has widely used this mathematical technique on biological problems.⁽⁹⁾

Basically, this method breaks the object to be analyzed into many small elements. The finer the elements, the higher the potential accuracy since the smaller motion allows more accuracy with the assumptions of linearity which are used. Unfortunately, the cost goes up. Consequently, an

affordable yet sufficiently accurate compromise is sought. Presented in this report is the second version of the model. This model differs from the first version in that it is a three dimensional finite element model. (The previous model was two dimensional.) The three dimensional model provides a more accurate representation of the real world. The two dimensional model represents the objects, looking at stresses only in one plane. In the three dimensional model the basically rectangular and triangular shaped elements are cuboidal shaped elements, having depth. The object of interest can then be mathematically represented as a true three dimensional object. The model used for this study calculated stresses at three points along the edge of each element as well as in the center (or centroid) for a total of 21 points per element. Since stresses can be calculated along edges of elements, the interfacial stresses can be calculated.

The following elastic moduli were used in the three dimensional model: ceramic, 54.53×10^6 psi; gold, 11.92×10^6 psi; and bone, 1.98×10^6 psi. Also, rigid bonding was assumed at the interface. This assumption is considered reasonable, since the serrated shape closely modeled by the ingrown bone and ceramic surface roughness probably eliminates relative motion between bone and ceramic. Using these constraints, the data were computed for an axial (occlusal) static load of 25 pounds. These calculations are for the smallest implant (4 mm x 4 mm). This size implant would have the highest stresses under the serrations because it has the smallest surface area of serrations to distribute the load. Also, the wall thickness of ceramic would be the thinnest and most critical in this size implant.

Figure 14 is a grid representation of the three dimensional mathematical model of a full size implant. For simplicity, only one-half of the implant is shown in cross section. The relatively thin cortical plates of bone and the thin layer of bone below the implant are characteristics normally noted histologically. The outline of the implant indicates the area which is ceramic. The post area and the portion above the top of the implant is gold. The remaining area is bone. The stresses shown are those at the centroids or center of each three dimensional element.

In this, the maximum stresses in the bone are almost within the self-imposed 400 psi bone compressive stress limit.⁽⁹⁾ The bone stresses

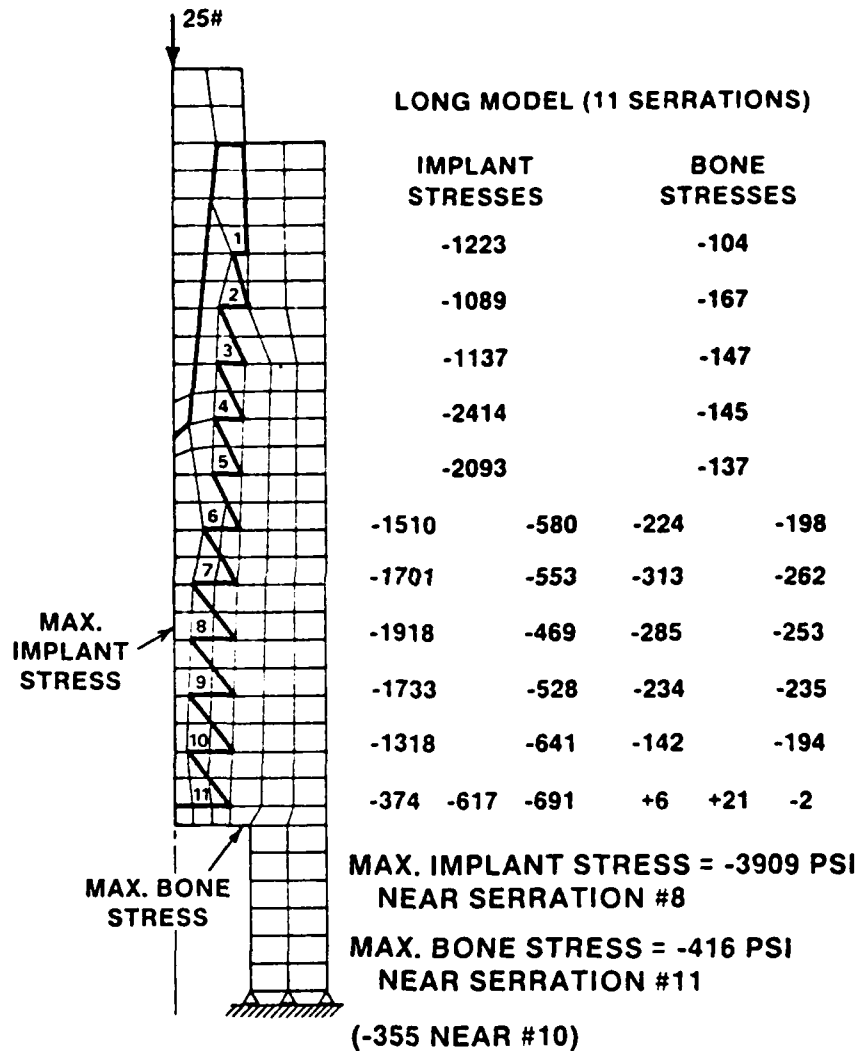


FIGURE 14. GRID REPRESENTATION OF THREE DIMENSIONAL AXISYMMETRIC MODEL OF 4 X 4 MM IMPLANT

In this figure, only one-half of the implant system is shown. The heavy line shows the outline of the ceramic implant. The stresses shown are those at the element centroids.

- is compression, + is tension

are somewhat higher than those predicted by the simpler two dimensional model reported in the 12th report.⁽²⁹⁾ The highest compressive stress is indicated may be due to the sharp angulation selected at that particular point.

Additionally, the node point stresses were calculated at the inner edge, center and tip of each serration. These are the bone stresses at the bone-ceramic interface. The bone node stresses were consistently, slightly lower than those calculated for the centroids. The stresses were also fairly uniform at the various positions along each serration. Also the model indicates fairly uniform stresses at various serration levels despite the differences in serration depth. However, the nodes indicated slightly higher stresses in the ceramic than their respective centroid (Table 1). The stresses decreased progressively from the implant axis. The agreement between the two modeling approaches supports the use of centroid stresses as reasonable representations of the actual stress.

Figure 15 is an additional case that was calculated with the implant shortened by three serrations. This model asks the practical question of stress alterations when an implant is shortened. In the case of group III implants, which are placed deeper than with groups I or II, frequently 3 serrations had to be sacrificed since limited vertical bone height was available to accept the implant. The centroid axial stresses at the interface are shown. The model suggests minimal changes in implant stresses, except at the point of maximal stress near the implant apex.

The maximum stress level is higher than the self imposed design limit, but it is a stress level still below that which will inevitably produce bone resorption.⁽⁹⁾ Consequently, even the shortened implant should be adequate to distribute the imposed stresses.

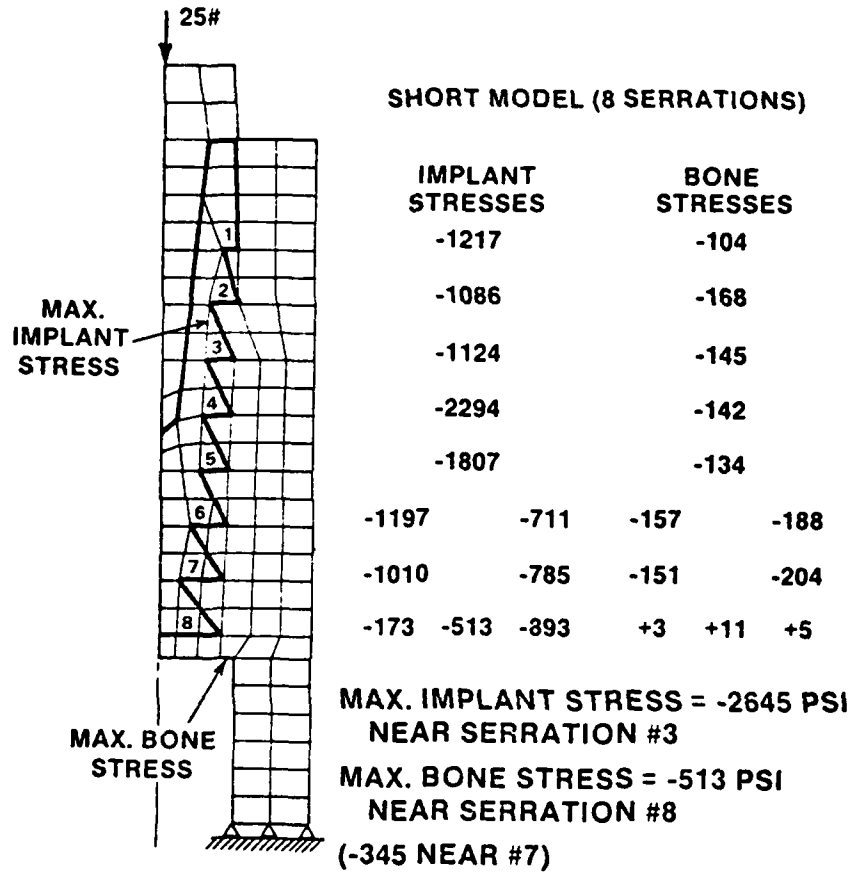


FIGURE 15. GRID REPRESENTATION OF SHORTENED 4 x 4 MM IMPLANT

The stresses at the element centroids are shown.

TABLE 1. NODE POINT STRESSES IN THREE DIMENSIONAL
AXISYMMETRIC MODEL

A long bottom edge of serration in ceramic

Serration Number	Inner Edge	Center			Tip	Serration Depth (mm)
1	-2390			-990	-992	0.435
2	-1114			-745	-383	0.763
3	-1676			-935	-205	0.761
4	-1625			-902	-193	0.759
5	-1602			-895	-201	0.762
6	-2769	-765		-500	-476	0.979
7	-2001	-574		-507	-527	1.196
8	-2973	-955		-487	-471	1.196
9	-2640	-803		-452	-458	1.197
10	-1688	-370		-378	-450	1.196
11	+247	+535	+339	+534	-22 -232	-120 2.956

NODE POINT STRESSES IN BONE ADJACENT TO
CERAMIC POINTS CALCULATED ABOVE

(These are compressive stresses in bone at the bone-ceramic interface.)

Serration Number	Inner Edge	Center			Tip
1	-92			-93	-94
2	-166			-161	-109
3	-149			-131	-113
4	-137			-125	-114
5	-130			-121	-113
6	-231	-189		-180	-168
7	-335	-264		-244	-222
8	-311	-241		-227	-214
9	-263	-197		-185	-198
10	-173	-114		-104	-169
11	-10	-36	-37	-45	-78 -114 -178

Note: All unit PSI
 - is compression
 + is tension

CONCLUSIONS

The animal research to date indicates a high probability of success for the implant system. Loss of stability via bone loss occurred in only one animal implant that has become stable. Most failures in baboons have been caused by fracture of ceramic at the approximate level of the alveolar crest. Fractures appear to be clustered in implants produced in 1976. Low-quality ceramic material is suggested. Contemporary materials now being used have vastly improved structural properties, and failures have not occurred with these newer materials.

The baboon studies now terminated provided valuable information as to long-term success of implants. The longest term implants provide proof that successful function of serrated ceramic implants is possible for up to eight years. There has been no evidence of any deleterious effect of the implant system upon the health of the animal by any of the indices measured.

This baboon study is the only known long-term animal trial of ceramic implants. The clinical chemistry, clinical health, and eventual necropsy data (both gross and microscopic) will be relevant to the human situation. One apparent drawback to the baboon model is the ease and rapidity of bone ingrowth relative to the human. However, once ingrowth has occurred, the baboon model provides a "worst case" long term test for the implant. Relatively high loadings and lack of oral hygiene are a severe test for the implants.

The human studies initially did not prove as successful as the baboon studies. Loss of initial stability of the implant appears to affect the long-term success. Even though all human implants were implanted stable by virtue of an interference fit with the bone, this stability was lost within the first month. In the successful cases, the relative degree of mobility reversed and continually decreased until minimal. However, in many of the implants, mobility slowly increased over a period of 1 to 2 years until failure was inevitable. In light of the loss of initial stability different stabilization techniques were attempted to rectify the situation. The most recently employed technique of placing the implant flush with alveolar bone has produced a dramatic change in the results. The extra isolation from

mechanical stresses appears to have made a significant difference in the outcome of the implant studies. Continued observation of present implants is required to validate this statement.

The initial ingrowth phase continues to be the most critical phase of the procedure. If initial stability is maintained throughout the bone ingrowth and reconstruction phase; the long-term prognosis for success is excellent.

RECOMMENDATIONS

It is recommended that the human study be continued to ascertain if the increased apparent success observed with flush placement of the implants (group III) can be continued. The maintenance of initial stability in a high percentage of this last group of implants is encouraging. Since initial stability appears to be a critical factor, techniques to facilitate initial stability should be incorporated. To this end, a regular shape (circular) implant should be considered to facilitate initial stabilization.

It is recommended that the parametric analysis of the implant in bone be continued. Specifically, lateral loading should be studied to ascertain fracture limits of the implant. Also serration distribution should be assessed to see if any improvement is possible.

It is recommended that the long-term animal evaluation be completed. An in-depth histopathologic analysis of all major organ systems should be completed, as well as the analysis of the implant-bone interface. Tissue samples (from various organ systems) should be evaluated for aluminum to ascertain the fate of alumina in the body.

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